Interventions


Deep brain stimulation for hyperkinetics disorders: dystonia, tardive dyskinesia, and tics.

Welter ML, Grabli D, Vidailhet M.


PURPOSE OF REVIEW: This review focuses on new insights in deep brain stimulation (DBS) for patients with hyperkinetic movement disorders: dystonia, tardive dyskinesia and Gille de la Tourette’s syndrome, during the last 18 months. RECENT FINDINGS: The recent literature confirms the efficacy of high-frequency stimulation of the globus pallidus internus (GPI) for primary dystonia, generalized or not, with a stable effect over time. The benefit of DBS in other forms of localized dystonia remains to be demonstrated in larger studies. Some clinical and radiological predictive factors have been determined with a predominant influence of the disease duration. Tardive dystonia and myoclonus-dystonia are also improved by GPI stimulation. Encouraging results obtained in cerebral palsy may pave the way for the application of DBS in other secondary dystonia. In Gilles de la Tourette’s syndrome, both stimulation of the centre-median/parafascicular nucleus of the thalamus and GPI stimulation (ventromedial) have demonstrated efficacy with stable long-term effect. Thalamic stimulation failed to improve obsessions and compulsions in some patients. Stimulation of the nucleus accumbens has been tested in few cases with contradictory efficacy. In both diseases, complications are rare with no major side effects. SUMMARY: The few controlled studies showed that bilateral GPI stimulation is a well tolerated and a long-term effective treatment for hyperkinetic disorders. However, recent published data of DBS applied in different targets or patients (especially secondary dystonia) are mainly uncontrolled case reports, precluding the clear determination of the efficacy of this procedure and the choice of the 'good' target for the 'good' patient.

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Neural Mechanism and Clinical Significance of the Plantar Grasp Reflex in Infants.

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The plantar grasp reflex can be elicited in all normal infants from 25 weeks of postconceptional age until the end of 6 months of corrected age according to the expected birth date. This reflex in human infants can be regarded as a rudiment of responses that were once essential for ape infants in arboreal life. The spinal center for this reflex is
probably located at the L(5)-S(2) levels, which, however, are controlled by higher brain structures. Nonprimary motor areas may exert regulatory control of the spinal reflex mechanism through interneurons. In infants, this reflex can be elicited as the result of insufficient control of the spinal mechanism by the immature brain. In adults, lesions in nonprimary motor areas may cause a release of inhibitory control by spinal interneurons, leading to a reappearance of the reflex. The plantar grasp reflex in infants is of high clinical significance. A negative or diminished reflex during early infancy is often a sensitive indicator of spasticity. Infants with athetoid type cerebral palsy exhibit an extremely strong retention of the reflex, and infants with mental retardation also exhibit a tendency toward prolonged retention of the reflex. Copyright © 2010 Elsevier Inc. All rights reserved.

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Evidence on physiotherapeutic interventions for adults with cerebral palsy is sparse. A systematic review.

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Objectives: To identify evidence evaluating the effectiveness of physiotherapy in adolescents (>16 years of age) and adults with cerebral palsy. Data sources: Systematic literature search from the earliest available time until March 2009. Additional studies were identified through reference and citation tracking. Review methods: Two reviewers independently agreed on eligibility, methodological quality and quality of evidence assessment. Standard methods were used for quality assessments. Results: Included were 13 studies, two of which were randomized controlled trials. No article met the criteria for high methodological quality. Evidence of moderate quality was found on gait after strength training. Evidence of low quality was found on balance after strength training and workstation interventions. Low-quality evidence was also found on functionality after strength training in four studies evaluating gross motor capacity. There was very low-quality evidence on increased muscle strength and in outcome measures used to evaluate range of motion. Conclusion: Evidence for the effect of physiotherapy on adolescents and adults with cerebral palsy is sparse, and therefore there is an urgent need for well-designed physiotherapeutic trials for these people.

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Modified constraint-induced movement therapy or bimanual occupational therapy following injection of Botulinum toxin-A to improve bimanual performance in young children with hemiplegic cerebral palsy: a randomised controlled trial methods paper.

Hoare BJ, Imms C, Rawicki HB, Carey L.

BACKGROUND: Use of Botulinum toxin-A (BoNT-A) for treatment of upper limb spasticity in children with cerebral palsy has become routine clinical practice in many paediatric treatment centres worldwide. There is now high-level evidence that upper limb BoNT-A injection, in combination with occupational therapy, improves outcomes in children with cerebral palsy at both the body function/structure and activity level domains of the International Classification of Functioning, Disability and Health. Investigation is now required to establish what amount and specific type of occupational therapy will further enhance functional outcomes and prolong the beneficial effects of BoNT-A.

METHODS: A randomised, controlled, evaluator blinded, prospective parallel-group trial. Eligible participants were children aged 18 months to 6 years, diagnosed with spastic hemiplegic cerebral palsy and who were able to demonstrate selective motor control of the affected upper limb. Both groups received upper limb injections of BoNT-A. Children were randomised to either the modified constraint-induced movement therapy group (experimental) or bimanual occupational therapy group (control). Outcome assessments were undertaken at pre-injection and 1, 3 and 6 months following injection of BoNT-A. The primary outcome measure was the Assisting Hand Assessment. Secondary outcomes include: the Quality of Upper Extremity Skills Test; Pediatric Evaluation of Disability Inventory; Canadian Occupational Performance Measure; Goal Attainment Scaling; Pediatric Motor Activity Log; modified Ashworth Scale and; the modified Tardieu Scale. DISCUSSION: The aim of this paper is to describe the methodology of a randomized controlled trial comparing the effects of modified constraint-induced movement therapy (a uni-
manual therapy) versus conventional occupational therapy (a bimanual therapy) on improving bimanual upper limb performance of children with hemiplegic cerebral palsy following upper limb injection of BoNT-A. The paper outlines the background to the study, the study hypotheses, outcome measures and trial methodology. It also provides a comprehensive description of the interventions provided. Trial Registration ACTRN1260500002684.

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Dynamic spasticity of plantar flexor muscles in cerebral palsy gait.

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OBJECTIVE: To quantify dynamic spasticity, i.e. the coupling between muscle-tendon stretch velocity and muscle activity during gait, of the gastrocnemius and soleus muscles in children with spastic cerebral palsy. DESIGN: Prospective, cross-sectional study. SUBJECTS: Seventeen ambulatory children with cerebral palsy with spastic calf muscles, and 11 matched typically developing children. METHODS: The children walked at 3 different speeds. Three-dimensional kinematic and electromyographic data were collected. Muscle-tendon velocities of the gastrocnemius medialis and soleus were calculated using musculoskeletal modelling. RESULTS: In typically developing children, muscles were stretched fast in swing without subsequent muscle activity, while spastic muscles were stretched more slowly for the same walking speed, followed by an increase in muscle activity. The mean ratio between peak activity and peak stretch velocity in swing was approximately 4 times higher in spastic muscles, and increased with walking speed. In stance, the stretch of muscles in typically developing children was followed by an increase in muscle activity. Spastic muscles were stretched fast in loading response, but since muscle activity was already built up in swing, no clear dynamic spasticity effect was present. CONCLUSION: Spastic calf muscles showed increased coupling between muscle-tendon stretch velocity and muscle activity, especially during the swing phase of gait.

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Functional reaching discloses perceptive impairment in diplegic children with cerebral palsy.

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The currently accepted definition classifies Cerebral Palsy (CP) as a mere posture and movement disorder. Conversely, some authors have recently associated the presence of several motor dysfunctions exhibited by diplegic children with CP to an impairment in the perceptive system. The aim of the present study was to investigate the influence of the Perceptive Impairment (PI) on motor control and to appraise if the PI can be revealed by a reaching task. A functional reach and touch experiment was accomplished from sitting posture considering different directions and distances. Typically developing and diplegic children with CP were enrolled and, the latter, a priori divided in two subgroups considering a positive or negative diagnosis of PI. The reaching trials were quantified by means of centre of pressure analysis in terms of the overall quality of the task, and accuracy and effectiveness of postural adjustments and Anticipatory Postural Adjustments (APAs). The three groups showed statistically significant differences in terms of percentage of touched target, and of time spent and maximum distance covered to reach the target. In particular, PI caused a major difficulty in accomplishing the reaching tasks, thus a lower autonomy level in action. Overall, the PI strongly affected the anticipatory control system. Children with PI, rarely recruited APAs, each of which was characterized by small amplitude and inaccuracy in direction. The lack of effective APAs indicated how PI strongly influenced the motor control strategy. The present study demonstrates that the PI is a primary syndrome responsible for the long-term prognosis beside the motor and the postural disorders in CP. Copyright © 2010 Elsevier B.V. All rights reserved.
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Multilevel botulinum toxin type a as a treatment for spasticity in children with cerebral palsy: a retrospective study.
Unlu E, Cevikol A, Bal B, Gonen E, Celik O, Kose G.
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INTRODUCTION: Cerebral palsy is the most common cause of physical disability in children. Spasticity is a disabling clinical symptom that is prevalent among patients suffering from cerebral palsy. The treatment of spasticity with botulinum toxin type A (BTX-A) is a well-established option in the interdisciplinary management of spasticity, providing focal reductions in muscle tone in cerebral palsy patients. OBJECTIVE: The aim of this retrospective study was to describe the effect of multilevel BTX-A injections in the lower extremities, focusing mainly on gross motor function and functional status in cerebral palsy patients. METHODS: Data from 71 cerebral palsy patients (64% male, 36% female, mean age 6.7 +/-3.2 years) were analyzed retrospectively. We used the Ashworth and Tardieu scales to evaluate the degree of spasticity. Motor function was measured by the Gross Motor Function Measure (GMFM-88), and functional status was classified by the Gross Motor Function Classification System (GMFCS I-V). Multilevel BTX-A injections were applied after sedation and with electrostimulation guidance. The evaluations were repeated every three months, and the patients were followed for six months. RESULTS: We found that the Ashworth and Tardieu scores decreased significantly at the three-month evaluation (p<0.05) but not at the six-month evaluation (p>0.05). Although the improvement in spasticity was not maintained at the six-month evaluation, GMFM-88 scores increased significantly at the three- and six-month assessments. GMFSC levels showed no change in the three- and six-month assessments. CONCLUSION: We believe that a single multilevel BTX-A injection reduces spasticity and improves motor function in children with cerebral palsy.

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Epidemiology / Aetiology / Diagnosis & Early Treatment

Please note: This is not yet a comprehensive outline of cerebral palsy prevention literature. It is expected that more research will be included when the search terms are expanded to include key terms other than "cerebral palsy". It is a work-in-progress and it will be expanded in coming months.

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While intraventricular administration of epidermal growth factor (EGF) expands the proliferation of neural stem/progenitor cells in the subventricular zone (SVZ), overexpression of brain-derived neurotrophic factor (BDNF) is particularly effective in enhancing striatal neurogenesis. We assessed the induction of striatal neurogenesis and consequent functional recovery after chronic infusion of BDNF and EGF in an adult animal model of neonatal hypoxic-ischemic (HI) brain injury. Permanent brain damage was induced in CD-1 (ICR) mice (P7) by applying the ligation of unilateral carotid artery and hypoxic condition. At 6 weeks of age, the mice were randomly assigned to groups receiving a continuous 2-week infusion of one of the following treatments into the ventricle: BDNF, EGF,
BDNF/EGF, or phosphate buffered saline (PBS). Two weeks after treatment, immunohistochemical analysis revealed an increase in the number of BrdU(+) cells in the SVZ and striata of BDNF/EGF-treated mice. The number of new neurons co-stained with BrdU and betatubulin was also significantly increased in the neostriata of BDNF/EGF-treated mice, compared with PBS group. In addition, the newly generated cells were expressed as migrating neuroblasts labeled with PSA-NCAM or doublecortin in the SVZ and the ventricular side of neostriata. The new striatal neurons were also differentially as mature neurons co-labeled with BrdU(+)NeuN(+) . When evaluated postsurgical 8 weeks, BDNF/EGF-treated mice showed significantly longer rotarod latencies at constant speed (48 rpm) and under accelerating condition (4-80 rpm), relative to PBS and untreated controls. In the forelimb-use asymmetry test, BDNF/EGF-treated mice showed significant improvement in the use of the contralateral forelimb. In contrast, this BDNF/EGF-associated functional recovery was abolished in mice receiving a co-infusion of 2% cytosine-b-d-arabinofuranoside (Ara-C), a mitotic inhibitor. Induction of striatal neurogenesis by the intraventricular administration of BDNF and EGF promoted functional recovery in an adult animal model of neonatal HI brain injury. The effect of Ara-C to completely block functional recovery indicates that the effect may be the result of newly generated neurons. Therefore, this treatment may offer a promising strategy for the restoration of motor function for adults with cerebral palsy (CP). Published by Elsevier Ltd.

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Infantile Spasms: Does Season Influence Onset and Long-Term Outcome?
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To study whether onset of infantile spasms manifests seasonal variation, as previously reported, and whether any such seasonality is associated with treatment response and long-term outcome, data for 57 patients were retrospectively reviewed. The data were collected from hospital files and through a mail survey of children with infantile spasms born from 1980 to 2002 and monitored at the University Children's Hospital of Berne, Switzerland. The mean age at time of onset of infantile spasms was 7 months (range, 0.75-40), at diagnosis 8 months (range, 1-42) and at follow-up 11.3 years (range, 1-23 years). In 77% of participants, the etiology of infantile spasms was known (symptomatic); in the remaining 23% it was not known (nonsymptomatic). In contrast to previous findings, onset of infantile spasms was not associated with calendar month, photoperiod, or global solar radiation. Long-term prognosis was poor: 4 of the 57 (7%) children died; 49 (86%) had cognitive impairment and 40 (70%) had physical impairment; 31 (54%) had cerebral palsy, 37 had (65%) persistent seizures, and 9 (16%) had Lennox-Gastaut syndrome. Symptomatic infantile spasms were associated with worse cognitive outcome (P < 0.001), but treatment modality and overall duration of infantile spasms were not. There was no association of calendar month or photoperiod at onset with cognitive outcome or treatment response. Copyright © 2010 Elsevier Inc. All rights reserved.

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10. Early Hum Dev. 2010 Jul 5. [Epub ahead of print]
Does perinatal asphyxia contribute to neurological dysfunction in preterm infants?
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BACKGROUND: Children born preterm are known to be at risk for neurodevelopmental disorders. The role of perinatal asphyxia in this increased risk is still a matter of debate. AIM: To analyze the contribution of perinatal asphyxia in a population of preterm infants admitted to a secondary paediatric setting to neurological dysfunction in the first months after birth and to the development of cerebral palsy. METHODS: 17 preterm infants with perinatal asphyxia born before 35 weeks postmenstrual age (PMA) and 34 carefully matched preterm controls without asphyxia were studied. Neuromotor outcome was examined by means of three assessments of the quality of general movements (GM) at "preterm" (around 34 weeks PMA), "writhing" (around term age) and "fidgety" GM age (around 3 months post term). Follow-up until at least 18 months corrected age focused on the presence of cerebral palsy...
(CP). RESULTS: GM-quality of infants with asphyxia and of those without did not differ. Multivariate analysis revealed that abnormal GMs at "preterm" age were associated with respiratory problems, those at "writhing" age with none of the assessed risk factors, and those at "fidgety" age with the severity of periventricular leukomalacia (PVL) on neonatal ultrasound scan. Perinatal asphyxia was not associated with the development of CP. CP was associated with PVL and the presence of abnormal GMs at "fidgety" age. CONCLUSION: Perinatal asphyxia in preterm infants is not associated with an increased risk for neurodevelopmental problems including CP. Respiratory problems during the neonatal period are associated with PVL and adverse neurological outcome. Copyright © 2010. Published by Elsevier Ireland Ltd.

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Adverse obstetric events are associated with significant risk of cerebral palsy.

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OBJECTIVE: To examine adverse birth events on the development of cerebral palsy in California. STUDY DESIGN: A retrospective population-based study of children with cerebral palsy (as of Nov. 30, 2006), matched to their maternal/infant delivery records (Jan. 1, 1991 to Dec. 31, 2001) was performed. Demographic data and intrapartum events were examined. Six adverse birth-related events were chosen. Children without cerebral palsy were controls. RESULTS: There were 7242 children who had cerebral palsy (59% term) and 31.3% had 1 or more of the 6 adverse intrapartum events (12.9% in controls P < .0001). This held for both term (28.3% vs 12.7% controls) and preterm (36.8% vs 15.9%, controls) neonates (both P < .0001). Maternal (15.1% vs 6.6%) and neonatal (0.9% vs 0.1%) infection were increased in cerebral palsy cases (P < .0001). CONCLUSION: Almost one-third of children with cerebral palsy had at least 1 adverse birth-related event. Higher rates in the preterm group may partially explain the higher rates of cerebral palsy in this group. Copyright © 2010 Mosby, Inc. All rights reserved.

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Neurodevelopment of Extremely Preterm Infants who had Necrotizing Enterocolitis with or without Late Bacteremia.

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OBJECTIVE: To evaluate neurodevelopment after necrotizing enterocolitis (NEC) and late bacteremia, alone and together. STUDY DESIGN: Sample included 1155 infants born at 23 to 27 weeks' gestation. NEC was classified by the modified Bell's staging criteria and grouped as medical NEC or surgical NEC. Late bacteremia was defined as a positive blood culture result after the first postnatal week. Neurodevelopment was assessed at 24 months corrected age. Multivariable models estimated the risk of developmental dysfunction and microcephaly associated with medical or surgical NEC with and without late bacteremia. RESULTS: Children who had surgical NEC unaccompanied by late bacteremia were at increased risk of psychomotor developmental indexes <70 (OR = 2.7 [1.2, 6.4]), and children who had both surgical NEC and late bacteremia were at increased risk of diparetic cerebral palsy (OR = 8.4 [1.9, 39]) and microcephaly (OR = 9.3 [2.2, 40]). In contrast, children who had medical NEC with or without late bacteremia were not at increased risk of any developmental dysfunction. CONCLUSION: The risk of neurodevelopmental dysfunction and microcephaly is increased in children who had surgical NEC, especially if they also had late bacteremia. These observations support the hypothesis that bowel injury might initiate systemic inflammation potentially affecting the developing brain. (J Pediatr 2010;157:***). Copyright © 2010 Mosby, Inc. All rights reserved.

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Neural evidence for impaired action selection in right hemiparetic cerebral palsy.

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Recent studies suggest that in addition to low-level motor impairments, individuals with Hemiparetic Cerebral Palsy (HCP) are characterized by anticipatory action planning deficits as well. In the present EEG study we investigated the neural and temporal dynamics of action planning in participants with right-sided HCP (n=10) and in left-handed control subjects (n=10). An anticipatory planning task was used in which participants were required to grasp and rotate a hexagonal knob over different angles (60 degrees, 120 degrees or 180 degrees). At a behavioral level, participants with HCP were slower in their movements and often selected an inappropriate grip when grasping the object. At a neural level, individuals with HCP showed a strong reduction in the amplitude of the P2 component, likely reflecting an impaired process of action selection. In addition, a strong correlation was observed between the P2 amplitude and grasping and rotation times. The P2 component was localized to sources in the dorsal posterior cingulate cortex (dPCC), an area that is known to be involved in orienting visual body parts in space. Together these findings suggest that anticipatory planning deficits in cerebral palsy arise mainly due to an impaired process of action selection. Copyright © 2010. Published by Elsevier B.V.

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Phenotypic definitions of the cerebral palsies and the relationship to pathogenesis and the possibilities of prevention.

Neville B.

Comment on:

PMID: 20457711 [PubMed - indexed for MEDLINE]


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We demonstrate the utility of functional near-infrared spectroscopy (fNIRS) as a tool for physicians to study cortical plasticity in children with cerebral palsy (CP). Motor cortex activation patterns were studied in five healthy children and five children with CP (8.4 +/- 2.3 years old in both groups) performing a finger-tapping protocol. Spatial (distance from center and area difference) and temporal (duration and time-to-peak) image metrics are proposed as potential biomarkers for differentiating abnormal cortical activation in children with CP from healthy pediatric controls. In addition, a similarity image-analysis concept is presented that unveils areas that have similar activation patterns as that of the maximum activation area, but are not discernible by visual inspection of standard activation images. Metrics derived from the images presenting areas of similarity are shown to be sensitive identifiers of abnormal activation patterns in children with CP. Importantly, the proposed similarity concept and related metrics may be applicable to other studies for the identification of cortical activation patterns by fNIRS.
Isolated ischaemic lesions in the foot motor area mimic peripheral lower-limb palsy.
PMID: 20581145 [PubMed - indexed for MEDLINE]

Neurological picture. MRI of metronidazole induced cerebellar ataxia.
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